CLAIMS

1. A pharmaceutical composition comprising sodium 4-phenylbutyrate, an effective amount of at least one aromatic flavoring agent, and an effective amount of at least one synthetic sweetening agent.

2. A pharmaceutical composition according to claim 1, in which the aromatic flavoring agent is selected from fruit flavoring agents.

3. A pharmaceutical composition according to claim 2, in which the aromatic flavoring agent is a strawberry flavoring agent.

4. A pharmaceutical composition according to claim 1, in which the synthetic sweetening agent comprises at least one synthetic sweetening agent selected from aspartame and potassium acesulfame.

5. A pharmaceutical composition according to claim 1, in which the synthetic sweetening agent comprises a mixture of aspartame and potassium acesulfame.

6. A pharmaceutical composition according to claim 1, in which the sodium 4-phenylbutyrate is present in the form of granules which further comprise an effective amount of a binding agent.

7. A pharmaceutical composition according to claim 6, which comprises, per 100 parts by dry weight of the composition;

from about 80 to about 90 parts by weight of sodium 4-phenylbutyrate;

from about 3.5 to about 5.0 parts by weight of aspartame;

from about 1.5 to about 3.5 parts by weight of potassium acesulfame;

from about 2.5 to about 5.0 parts by weight of an aromatic fruit flavoring agent; and

from about 3.5 to about 6.5 parts by weight of a binding agent.

8. A pharmaceutical composition according to claim 7, in which the binding agent is polyvinylpyrrolidone.

9. A pharmaceutical composition according to claim 7, in which the fruit flavoring agent is a strawberry flavoring agent.

10. A dry powder pharmaceutical composition comprising sodium 4-phenylbutyrate, an effective amount of at least one water soluble sweetening agent, and an effective amount of at least one water soluble flavoring agent, the effective amounts being selected so as to mask substantially the bitter taste and pungent odor of sodium 4-phenylbutyrate.

11. A pharmaceutical composition which comprises granules comprising sodium 4-phenylbutyrate, a binding agent, an effective amount of at least one synthetic water soluble sweetening agent, and an effective amount of at least one water soluble flavoring agent, the effective amounts being selected so that, upon dissolution in water to yield an aqueous solution that contains from about 10 to about 50 mg/ml of sodium 4-phenylbutyrate, the resulting aqueous solution is palatable.

12. A pharmaceutical composition according to claim 11, which comprises per 100 parts by weight of the composition;

from about 80 to about 90 parts by weight of sodium 4-phenylbutyrate;

from about 3.5 to about 5.0 parts by weight of aspartame;

from about 1.5 to about 3.5 parts by weight of potassium acesulfame;

from about 2.5 to about 5.0 parts by weight of a strawberry flavoring agent; and

from about 3.5 to about 6.5 parts by weight of polyvinylpyrrolidone.

13. A concentrated aqueous solution containing at least about 200 mg/ml of sodium 4-phenylbutyrate up the solubility limit thereof measured at 10°C, and having dissolved therein an effective amount of at least one water soluble sweetening agent, and an effective amount of at least one water soluble flavoring agent, the effective amounts being selected so as to mask substantially, following dilution by at least about 5 fold up to about 10 fold or more with water, the bitter taste and pungent odor of sodium 4-phenylbutyrate.

14. A concentrated aqueous solution according to claim 13, in which the flavoring agent is selected from fruit flavoring agents.

15. A concentrated aqueous solution according to claim 13, in which the flavoring agent is a strawberry flavoring agent.

16. A concentrated aqueous solution according to claim 13, in which the synthetic sweetening agent comprises at least one synthetic sweetening agent selected from aspartame and potassium acesulfame.

17. A concentrated aqueous solution according to claim 13, in which the synthetic sweetening agent comprises a mixture of aspartame and potassium acesulfame.

18. A concentrated aqueous solution according to claim 13, which comprises, per 100 parts by weight of the dry components of the composition;

from about 80 to about 90 parts by weight of sodium 4-phenylbutyrate;

from about 3.5 to about 5.0 parts by weight of aspartame;

from about 1.5 to about 3.5 parts by weight of potassium acesulfame;

from about 2.5 to about 5.0 parts by weight of a fruit flavoring agent; and

from about 3.5 to about 6.5 parts by weight of polyvinylpyrrolidone.

19. A concentrated aqueous solution according to claim 17, in which the fruit flavoring agent is a strawberry flavoring agent.

20. A unit dose for administration to a patient requiring treatment for a urea cycle deficiency according to a regime in which the patient is administered a predetermined number of doses daily corresponding to from about 450 to about 600 mg/kg/day of sodium 4-phenylbutyrate, the unit dose prepared by diluting with water an aliquot of a concentrated aqueous solution containing at least about 200 mg/ml of sodium 4-phenylbutyrate up the solubility limit thereof measured at 10°C, an effective amount of at least one water soluble sweetening agent, and an effective amount of at least one water soluble flavoring agent, the unit dose containing from about 10 to about 50 mg/ml of sodium 4-phenylbutyrate and the effective amounts being selected so as to mask substantially the bitter taste and pungent odor of sodium 4-phenylbutyrate.

21. A unit dose according to claim 20, in which the amount of sodium 4-phenylbutyrate corresponds to no more than about one third of the maximum daily requirement of about 600 mg/kg/day.

22. A pharmaceutically acceptable aqueous solution ready for administration to a patient requiring treatment for a urea cycle deficiency according to a regime in which the patient is administered a predetermined number of doses daily corresponding to from about 450 to about 600 mg/kg/day of sodium 4-phenylbutyrate, the solution containing a unit dose of sodium 4-phenylbutyrate, an amount of at least one water soluble sweetening agent, and an amount of at least one water soluble flavoring agent,

the concentration of sodium 4-phenylbutyrate in the aqueous solution ranging from about 10 to about 50 mg/ml and the amounts of the at least one water soluble sweetening agent and of the at least one water soluble flavoring agent being selected so as to mask substantially the bitter taste and pungent odor of sodium 4-phenylbutyrate.

23. A pharmaceutical composition comprising granules comprising sodium 4-phenylbutyrate and a binding amount of a binding agent, the composition further including an effective amount of at least one synthetic water soluble sweetening agent, and an effective amount of the at least one water soluble flavoring agent, the amounts of at least one artificial water soluble sweetening agent and of the at least one water soluble flavoring agent being sufficient upon dissolution in water to yield an aqueous solution containing from about 10 to about 50 mg/ml of sodium 4-phenylbutyrate to render the resulting aqueous solution palatable to a child.

24. A pharmaceutical composition according to claim 23, in which the binding agent comprises polyvinylpyyrolidone.

25. A pharmaceutical composition according to claim 23, in which the flavoring agent is selected from fruit flavoring agents.

26. A pharmaceutical composition according to claim 25, in which the flavoring agent is a strawberry flavoring agent.

27. A pharmaceutical composition according to claim 23, in which the synthetic sweetening agent comprises at least one synthetic sweetening agent selected from aspartame and potassium acesulfame.

28. A pharmaceutical composition according to claim 23, in which the synthetic sweetening agent comprises a mixture of aspartame and potassium acesulfame.

29. A pharmaceutical composition according to claim 23, which comprises, per 100 parts by dry weight of the composition;

from about 82.5 to about 99.5 parts by weight of sodium 4-phenylbutyrate;

from about 3.25 to about 4.5 parts by weight of aspartame;

from about 1.75 to about 3.25 parts by weight of potassium acesulfame;

from about 3.25 to about 4.5 parts by weight of a water soluble fruit flavoring agent; and

from about 3.25 to about 5.25 parts by weight of polyvinylpyrrolidone.

30. A pharmaceutical composition according to claim 29, in which the fruit flavoring agent is a strawberry flavoring agent.

31. A pharmaceutical composition according to claim 23, wherein the granules comprise sodium 4-phenylbutyrate and the binding agent and wherein the granules are mixed with the at least one synthetic water soluble softening agent and with the at least one water soluble flavoring agent to form the wetted mass.

32. A pharmaceutical composition according to claim 23, wherein the granules comprise sodium 4-phenylbutyrate, the binding agent, the at least one synthetic water soluble sweetening agent and the at least one water soluble flavoring agent.

33. In a method of treating a patient suffering from a condition selected from a urea cycle deficiency and sickle-cell anaemia which comprises administering to the patient in one or more unit doses daily a pharmaceutical composition comprising sodium 4-phenylbutyrate in an

amount corresponding to from about 450 to about 600 mg/kg/day, the improvement comprising administering sodium 4-phenylbutyrate in the form of an aqueous solution comprising sodium 4-phenylbutyrate, an effective amount of at least one water soluble sweetening agent, and an effective amount of at least one water soluble fruit flavoring agent, the effective amounts being selected so as to mask substantially the bitter taste and pungent odor of sodium 4-phenylbutyrate.

34. A method according to claim 33, in which the fruit flavoring agent is a strawberry flavoring agent.

35. A method according to claim 33, in which the synthetic sweetening agent comprises at least one synthetic sweetening agent selected from aspartame and potassium acesulfame.

36. A method according to claim 33 in which the synthetic sweetening agent comprises a mixture of aspartame and potassium acesulfame.

37. A method according to claim 36, in which the amounts of aspartame and potassium acesulfame are selected so as not to exceed their respective Acceptable Daily Intakes.

38. A method according to claim 33, in which the composition comprises, per 100 parts by dry weight of the composition:

from about 80 to about 90 parts by weight of sodium 4-phenylbutyrate;

from about 3.5 to about 5.0 parts by weight of aspartame;

from about 1.5 to about 3.5 parts by weight of potassium acesulfame;

from about 2.5 to about 5.0 parts by weight of a fruit flavoring agent; and

from about 3.5 to about 6.5 parts by weight of a binding agent.

39. A method according to claim 38, in which the fruit flavoring agent is a strawberry flavoring agent.

40. A method according to claim 33, in which the unit dose is prepared by diluting with water a concentrated aqueous solution containing at least about 200 mg/ml of sodium 4-phenylbutyrate up the solubility limit thereof measured at 10°C, an effective amount of at least one water soluble sweetening agent, and an effective amount of at least one water soluble flavoring agent, the effective amounts being selected so as to mask substantially, following dilution by from about 5 times up to about 10 times or more with water, the bitter taste and pungent odor of sodium 4-phenylbutyrate.

41. A method according to claim 40, in which the at least one water soluble flavoring agent is selected from fruit flavoring agents.

42. A method according to claim 41, in which the at least one water soluble flavoring agent comprises a strawberry flavoring agent.

43. A method according to claim 40, in which the synthetic sweetening agent comprises at least one synthetic sweetening agent selected from aspartame and potassium acesulfame.

44. A method according to claim 40, in which the synthetic sweetening agent comprises a mixture of aspartame and potassium acesulfame.

45. A method according to claim 42, in which the concentrated aqueous solution comprises, per 100 parts by dry weight of the components;

from about 82.5 to about 88.5 parts by weight of sodium 4-phenylbutyrate;

from about 3.25 to about 4.5 parts by weight of aspartame;

from about 1.75 to about 3.25 parts by weight of potassium acesulfame;

from about 3.25 to about 4.5 parts by weight of an aromatic fruit flavoring agent; and

from about 3.25 to 5.25 parts by weight of a binding agent.

46. A method according to claim 45, in which the binding agent comprises polyvinylpyrrolidone.

47. A method according to claim 33, in which the patient is administered three unit doses daily and in which the amount of sodium 4-phenylbutyrate in the unit dose corresponds to no more than about one third of the maximum daily requirement of about 600 mg/kg/day.

48. A method according to claim 45, in which the condition is a urea cycle deficiency.

49. A method according to claim 45, in which the condition is sickle-cell anaemia.

50. A method of manufacturing a pharmaceutical composition comprising sodium 4-phenylbutyrate, the method comprising:

(i) providing a solution of a binding agent in a volatile solvent therefor;

(ii) admixing a predetermined volume of the solution of the binding agent with a predetermined quantity of sodium 4-phenylbutyrate to form a wetted mass;

(iii) forming the wetted mass into granules;

(iv) drying the granules to remove essentially all of the volatile solvent therefrom and form dry granules; and

further including the step of incorporating into the composition an effective amount of at least one synthetic water soluble sweetening agent and an effective amount of at least one water soluble flavoring agent to form a pharmaceutical composition;

wherein the effective amounts are selected so that, upon dissolution of the pharmaceutical composition in

water to form a solution containing from about 10 to about 50 mg/ml of sodium 4-phenylbutyrate, the bitter taste and pungent odor of sodium 4-phenylbutyrate is effectively masked.

51. A method according to claim 50, wherein the admixing step (ii) comprises admixing the predetermined volume of the solution of the binding agent with the predetermined quantity of sodium 4-phenylbutyrate, with the effective amount of the at least one synthetic water soluble sweetening agent, and with the effective amount of the at least one water soluble flavoring agent to form the wetted mass.

52. A method according to claim 50, wherein the dry granules of step (iv) are mixed with the effective amount of the at least one synthetic water soluble sweetening agent and with the effective amount of the water soluble flavoring agent.

53. A method according to claim 50, in which the water soluble flavoring agent is a fruit flavoring agent.

54. A method according to claim 50, in which the water soluble flavoring agent is a strawberry flavoring agent.

55. A method according to claim 50, in which the synthetic sweetening agent comprises at least one synthetic sweetening agent selected from aspartame and potassium acesulfame.

56. A method according to claim 50, in which the synthetic sweetening agent comprises a mixture of aspartame and potassium acesulfame.

57. A method according to claim 50, in which the composition comprises, per 100 parts by dry weight of the composition:

from about 80 to about 90 parts by weight of sodium 4-phenylbutyrate;

from about 3.5 to about 5.0 parts by weight of aspartame;

from about 1.5 to about 3.5 parts by weight of potassium acesulfame;

from about 2.5 to about 5.0 parts by weight of a fruit flavoring agent; and

from about 3.5 to about 6.5 parts by weight of a binding agent.

58. A method according to claim 57, in which the fruit flavoring agent is a strawberry flavoring agent.

59. A method according to claim 50, in which the volatile solvent is iso-propyl alcohol.

60. A method according to claim 59, in which the granules are dried at a temperature of from about 40 to about 60°C.

61. A method according to claim 60, in which the granules are dried at a temperature of about 50°C.

62. A method according to claim 50, in which the binding agent is polyvinylpyrrolidone.